

THE FOLLOWING TWO PAGES SHOWS A MARKED UP VERSION OF
PAGE ONE OF THE SPECIFICATION

TREATMENT OF METHOD FOR TREATING NEUROMUSCULAR
DISORDERS AND CONDITIONS WITH DIFFERENT BOTULINUM TOXIN
TYPES A AND B SEROTYPE

CROSS REFERENCE

This application is a continuation of serial number
08/075,048, filed June 10, 1993.

FIELD OF THE INVENTION

The present invention provides novel methods for treating diseases of the nervous system, e.g., neuromuscular disorders and conditions, with botulinum toxins. In addition, the present invention provides methods useful in all tissue and organ systems which involve the release of neurotransmitters, especially acetylcholine. These cholinergic transmission systems include neuromuscular junctions (muscles), smooth muscles (gut, sphincters, etc.) and secretions (salivation and mucus).

BACKGROUND OF THE INVENTION

A bacterial toxin, botulinum toxin, in particular botulinum toxin type A, has been used in the treatment of a number of neuromuscular disorders and conditions involving muscular spasm; for example, strabismus, blepharospasm, spasmodic torticollis (cervical dystonia), oromandibular dystonia and spasmodic dysphonia (laryngeal dystonia). The toxin binds rapidly and strongly to presynaptic cholinergic nerve terminals and inhibits the exocytosis of acetylcholine by decreasing the frequency of acetylcholine release. This results in local

paralysis and hence relaxation of the muscle afflicted by spasm.

For one example of treating neuromuscular disorders, see U.S. Patent No. 5,053,005 to Borodic, which suggests treating curvature of the juvenile

**PLEASE REPLACE THE CLAIMS BY THE FOLLOWING UNMARKED
VERSION OF THE CLAIMS**

1. A method of treating a patient suffering from a neuromuscular disorder or condition, said method comprising administering to the patient a therapeutically effective amount of a botulinum toxin type A until the patient experiences loss of clinical response to the administered botulinum toxin and thereafter administering to the patient a botulinum toxin type B, said botulinum toxin type B being administered in therapeutically effective amounts.

4. A method of treating a patient suffering from a neuromuscular disorder or condition, said method comprising administration to the patient of a therapeutically effective amount of a botulinum toxin type A until the patient develops neutralizing antibodies and thereafter administering to the patient a botulinum toxin type B, said botulinum toxin type B being administered in a therapeutically effective amount.

11. The method of claim 1 or 4, wherein the neuromuscular disorder or condition is cervical dystonia.

12. A method of treating dystonia in a patient, wherein the patient has experienced a loss of or a diminished clinical effectiveness to the administration of a botulinum toxin type A, said method comprising administering to the patient a therapeutically effective amount of a botulinum toxin type B.

13. The method of claim 12, wherein the dystonia is cervical dystonia

14. The method of claim 13, wherein treating the cervical dystonia reduces the severity of an abnormal head position symptom of the cervical dystonia.

15. The method of claim 13, wherein treating the cervical dystonia reduces a neck pain associated with the cervical dystonia.

16. A method of treating dystonia in a patient, wherein the patient has developed neutralizing antibodies to a botulinum toxin type A, said method comprising administering to the patient a therapeutically effective amount of a botulinum toxin type B.

17. The method of claim 16, wherein the dystonia is cervical dystonia

18. The method of claim 17, wherein treating the cervical dystonia reduces the severity of an abnormal head position symptom of the cervical dystonia.

19. The method of claim 17, wherein treating the cervical dystonia reduces a neck pain associated with the cervical dystonia.

MARKED UP VERSION OF THE CLAIMS

1. A method of treating a patient suffering from a neuromuscular disorder or condition, said method comprising administering to the patient a therapeutically effective amount of a botulinum toxin type A ~~of a selected serotype~~ until the patient experiences loss of clinical response to the administered botulinum toxin and thereafter administering to the patient ~~another~~ a botulinum toxin type B ~~of a different serotype~~, said ~~another~~ botulinum toxin type B being administered in therapeutically effective amounts.

Cancel claim 2

Cancel claim 3

4. A method of treating a patient suffering from a neuromuscular disorder or condition, said method comprising administration to the patient of a therapeutically effective amount of a botulinum toxin type A ~~of a selected serotype~~ until the patient develops neutralizing antibodies and thereafter administering to the patient ~~another~~ a botulinum toxin type B ~~of a different serotype~~, said ~~another~~ botulinum toxin type B being administered in a therapeutically effective amount.

Cancel claims 5-10

Please add the following new claims 11-19:

11. The method of claim 1 or 4, wherein the neuromuscular disorder or condition is cervical dystonia.

12. A method of treating dystonia in a patient, wherein the patient has experienced a loss of or a diminished clinical effectiveness to the administration of a botulinum toxin type A, said method comprising administering to the patient a therapeutically effective amount of a botulinum toxin type B.

13. The method of claim 12, wherein the dystonia is cervical dystonia

14. The method of claim 13, wherein treating the cervical dystonia reduces the severity of an abnormal head position symptom of the cervical dystonia.

15. The method of claim 13, wherein treating the cervical dystonia reduces a neck pain associated with the cervical dystonia.

16. A method of treating dystonia in a patient, wherein the patient has developed neutralizing antibodies to a botulinum toxin type A, said method comprising administering to the patient a therapeutically effective amount of a botulinum toxin type B.

17. The method of claim 16, wherein the dystonia is cervical dystonia

18. The method of claim 17, wherein treating the cervical dystonia reduces the severity of an abnormal head position symptom of the cervical dystonia.

19. The method of claim 17, wherein treating the cervical dystonia reduces a neck pain associated with the cervical dystonia.